

PATENT APPLICATION
Navy Case No. 83,682

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION FOR LETTERS PATENT

TO ALL WHOM IT MAY CONCERN:

BE IT KNOWN THAT Dean Sribner of Arlington, VA, who is a citizen of the United States of America, has invented certain new and useful improvements in **"MICROELECTRONIC STIMULATOR ARRAY"** of which the following is a specification:

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MICROELECTRONIC STIMULATOR ARRAY

BACKGROUND OF THE INVENTION

Field of the Invention

This invention deals generally with neural prosthesis, specifically the concept of achieving a retinal prosthesis for blind patients through the creation of an electrical interface between a high-density electrode array and the curved surface of the retina.

Description of the Related Prior Art

There is a great deal of recent interest in the area of neural prosthesis, specifically the concept of achieving a retinal prosthesis for blind patients has been hypothesized by a number of researchers and is an active area of medical research. In a normal eye, in a basic concept **10**, **Figures 1a** and **1b** shows a ray trace of two photons **12** focused on a retina **21**. Note that the incoming photons **12** pass through several layers of transparent retinal cells **16** and **18** before being absorbed by the photoreceptors **22**. In a damaged eye, a retinal prosthesis device **24**, as shown in **Figures 1c** and **1d**, is positioned against the retina **21**. In this case, the photons **12** are absorbed by a microelectronic stimulating array or device **26** that is hybridized to a glass piece **28** containing an embedded array of microwires. The glass has a curved surface that conforms to the inner radius of the retina **21**. The microelectronic imaging device **26** is made of thin silicon containing very large scale integrated (VSLI) circuitry and photon detectors that convert the

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5 incident photons 12 to an electronic charge. The charge is then converted to a proportional amount of electronic current which is input to the nearby retinal cell layer 18. The cells fire and a signal is sent to the optic nerve 28.

A typical retinal prosthesis device combines two technologies: first, nanochannel glass (NGC) electrode arrays and secondly a two-dimensional (2-D) multiplexer array. NGC
10 technology employs fiber optic fabrication techniques to produce thin wafers of glass with very small channels perpendicular to the plane of the wafer. Typical NGC wafers that will be required for retinal prosthesis devices are several millimeters in diameter and can contain millions of channels with channel diameters on the order of one micron. The channels are filled with a good electrical conductor and one surface of the glass is ground to a spherical shape
15 consistent with the radius of curvature of the inside of the retina. The electrical conductors on the curved surface should protrude slightly to form efficient electrodes.

The 2-D multiplexer array is similar to infrared focal plane array (IRFPA) multiplexers that are microelectronic devices fabricated at silicon foundries. An IRFPA multiplexer is a 2-D array that reads out the infrared (IR) image captured by a complimentary detector array that
20 converts photons into electrical charge. The charge is integrated and stored in each unit cell for a few milliseconds. The full image is then multiplexed off the array at frame rates compatible with commercial video. For a retinal prosthesis test device that obtains its input image from an external camera, the process is essentially reversed and the device acts as a de-multiplexer. That is, the prosthesis devices will perform de-multiplexing operations, but will be referred to here

5 simply as a multiplexer.

The basic concept is straightforward: visual images can be produced in the brain by electrical stimulation of retinal cells. Two-dimensional arrays of retinal cells, such as ganglion or bipolar cells, can be stimulated using two-dimensional arrays of electrical impulses with the spatial form of an image. The axons of the ganglion cells then transmit the image through the optic nerve and on to the visual cortex. This is in lieu of the normal photo-transduction process that occurs in a healthy retina. In approximately 90 percent of blind patients, the photoreceptors are diseased, but the other retinal layers are still responsive to electrical stimulation.

Experimental test procedures, such as shown in **Figure 2**, use standard retinal surgical techniques performed in an operating room environment by an ophtalmologist. It is necessary that the patient be administered local anesthesia rather than general anesthesia so that visual perceptions can be orally recorded during the procedure.

There are a number of technical issues to be addressed in designing and fabricating a retinal prosthesis device, particularly if the device is to generate a high resolution image. First, there is the issue of creating an electrical interface between the high-density electrode array and the curved surface of the retina. The electrode array must have a spherical, convex shape in order to conform to the spherical concave surface of the retina. The electrode array must be bio-compatible and safe for permanent implantation. Second, the electrical stimulation pulse shapes and repetition rates, while generally well known, may need to be optimized for each individual recipient of a prosthesis device. The pulse amplitude is of course modulated within the retina to be proportional to the pixel value. Third, direct electrical stimulation of the ganglion

5 cells precludes certain image processing functions that normally would have occurred in earlier layers of the retina. Therefore, computationally based image preprocessing operations may need to be performed on the image before stimulation of the retina. Fourth, supplying power to a permanent implant will need to be engineered in a manner such that there are no wires or cables through the eye wall. Fifth, because a normal retina processes image information created by the photoreceptors in a simultaneous manner, it is assumed that a prosthesis device should similarly
10 excite retinal cells in a simultaneous manner, as opposed to sequential raster scan that might cause synchronicity problems downstream in the lateral geniculate nucleus (LGN) or visual cortex.

15 **SUMMARY OF THE INVENTION**

An object of this invention is to provide a device for achieving a retinal prosthesis for blind patients.

Another object of this invention is to provide a retinal prosthesis test device for providing visual images to the brain during acute human experiments to achieve electrical stimulation of
20 the retina tissue.

Another object of this invention is to provide a device for implant into the human eye that will allow electrical stimulation of the retinal or any neural tissue so as to provide visual images to the brain.

These and other objects are accomplished by the retinal prosthesis test device and retinal
25 implant device comprising two basic technologies -- nanochannel glass (NGC) electrode arrays

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5 and infrared focal plane array (IRFPA) multiplexers. In the retinal prosthesis test device, the device is positioned against the retina using standard retinal surgical techniques in an operating room environment. The device is comprised of a thin wafer of glass (NGC) with very small channels perpendicular to the plane of the wafer. The channels are filled with a good electrical conductor forming microwires with one surface of the glass being ground to a spherical shape
10 consistent with the radius of curvature of the inside of the retina. Electrical conductors protrude slightly from the NGC on the curved surface to form electrodes. The NGC is hybridized to a silicon IRFPA multiplexer using indium bump bonds. An image is serially input into the multiplexer via a very narrow, flexible micro-cable. The multiplexer is mounted on a ceramic carrier such that interconnecting bond pads on each are in close proximity to one another. A
15 video image is read into each of the unit cells on the multiplexer in pixel-by-pixel manner. Discrete samples of the analog video are input and stored as electrical charge on a MOS capacitor. After all unit cells have been loaded with the pixel values for the current frame, a biphasic pulse is sent through each unit cell and into the corresponding area of the retina. The biphasic pulse is modulated in proportion to the pixel value stored therein. Because the biphasic
20 pulse flows in parallel from a global external connection, the adjacent retinal neurons are all stimulated simultaneously, analogous to image photons stimulating photoreceptors in a normal retina.

A permanent retinal implant device uses an NGC array hybridized to a silicon chip in an identical manner to the retinal prosthesis test device, however, the image is no longer
25 multiplexed onto the chip through a wire from an external camera, but instead, the image is

5 simultaneously generated within each cell through a photon-to-electron conversion using a
silicon photodiode. The photons propagate directly into the backside of the device. Electrical
power and any control signals are transmitted through an inductively driven coil or antenna on
the chip. The device collects the charge in storage capacitors via the photon-to-electron
conversion process, stimulates the neural tissue with biphasic pulses in proportion to the stored
10 charges, and resets the storage capacitors to repeat the process.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1a shows a general diagram of a ray trace of photons incident on a retina without
a prosthesis device (a normal eye).

Figure 1b shows an interior view of a ray trace of photons incident on a retina without a
prosthesis device (a normal eye).

Figure 1c shows a general diagram of a ray trace of photons incident on a retina with a
prosthesis device (prosthesis device positioned against the retina).

Figure 1d shows an interior view of a ray trace of photons incident on a retina with a
prosthesis device (prosthesis device positioned against the retina).

Figure 2 shows a retinal prosthesis test device positioned against a retina.

Figure 3a shows a side-view of a fully packaged retinal prosthesis test device.

Figure 3b shows an enlarged view of a nano-channel glass (NCG) electrode array.

Figure 4 shows a conceptual layout (floor plan) of a silicon chip for the retinal test

5 prosthesis.

Figure 5 shows a conceptual design of a unit cell for the retinal prosthesis test device showing the external inputs from off-chip.

Figure 6 shows a block diagram of ancillary electronics for the retinal prosthesis test device.

10 **Figure 7** shows a side-view of a permanent implant device.

Figure 8 shows a conceptual design of a unit cell for a permanent implant device.

Figure 9 shows a conceptual layout (floor plan) of a silicon chip for a permanent implant device.

15 **DESCRIPTION OF THE PREFERRED EMBODIMENT**

In the preferred embodiment of a retinal prosthesis test device utilizing a microelectronic stimulator array **30**, as shown in **Figure 3a**, the nanochannel glass (NGC) electrode arrays **32** is hybridized to silicon multiplexer **34** using indium bump bonds, a technique from infrared (IR) focal plane array (IRFPA) multiplexers. An image is serially input onto the multiplexer **34** via a very narrow, flexible micro-cable **36**. The micro-cable **36** is approximately six inches in length and is custom made using gold leads patterned on polyimide strips. A ceramic carrier **38** with gold-filled via holes **42** provides a mechanically convenient means of routing interconnects from the top-side **44** of the ceramic carrier to the back-side **46**. By designing the ceramic carrier such that the top-side contacts to the via-holes **44** are in close proximity to bond pads **48** on the silicon

5 multiplexer **34**, the interconnection may be made with conventional tab-bonds **52** (thin gold ribbons fused to interconnects with mechanical pressure as is common practice in the microelectronics industry and is well known to those skilled in the art. This keeps all of the interconnects **52** from protruding above the spherical curved envelop defined by the polished NCG **32** and therefore prevents damage to the tab bond interconnects **52** or to a patients retina

10 **54.** A critical issue for any neural prosthesis device is biocompatibility and safety. Because the duration of any tests with the retinal prosthesis test device **30** are very short (less than an hour), biocompatibility issues are primarily reduced to acute effects of the testing and need not address the more difficult chronic issues that arise with permanent implants. Note that the surface of the packaging shown in **Figure 3a** consists only of glass **32** , platinum (Pt) electrodes **56** , and silicon
15 encapsulation **58**. However, as with any medical instrumentation, a major safety issue is electrical shock hazard. Note that the purpose of the device is to provide minimal electrical stimulation of retinal tissue using very low voltages and the smallest current possible, i.e., preferably about one volt and 1 μ A per unit cell for about 1 millisecond (every frame at a frame rate of 60 Hz). To protect a patient from any electrical shock, the patient is isolate from high
20 voltages using optocouplers (not shown) which are powered by low voltage electrical batteries (not shown), a technique well known to those skilled in the art.

Specific requirements for the NCG **32** are that the channels **56** making up the NCG **32**, as shown in **Figure 3b**, be small enough so that many microwires can be connected to each unit cell of the multiplexer array. This is for redundancy and to help simplify the hybridization alignment.

5 If the NCG wires were to approach the size of the unit cell, then a one-to-one alignment and hybridization would be required. This would be very problematic, because of irregularities in the NCG periodicity and the possibility of shorting nearest neighbor cells (not shown). On the other hand, very narrow channels **56** imply very high length-to-width aspect ratios of the channels **56** in the NCG **32**. This makes it difficult to fabricate large area NCG **32** samples with the proper
10 thickness. It is expected that a reasonable design size for the channels **56** should be on the order of a micron.

The NCG channels **56** must be filled with a high conductivity material **62**, such as platinum, to create microwires. Fabrication of the microwires can be performed using electrodeposition or infusion of molten metal under pressure, techniques that are well known to
15 those skilled in the art. After the channels **56** have been filled with conductive material and the continuity of the microwires has been confirmed, one side of the glass **32** must be polished to create a spherical surface **64**. This is accomplished by carefully grinding and polishing of the glass/metal composite. The radius of curvature is nominally half an inch in order to provide a conformal fit against the inside of the retina **54**. This is critically important as it allows
20 positioning of the high-density electrodes in the NCG **32** against the retinal **54** tissue. The polishing process will create slightly recessed microwires with respect to the curved NCG **32** surface. This is because the metal is softer than the glass. Therefore further processing may be necessary to create electrodes that protrude slightly above the curved surface **64** of the NCG **32**. In preparation for hybridizing the NCG **32** to the multiplexer **34**, or the microwires may be

5 hybridized directly to the indium bumps **66** on the multiplexer **34** or the glass is etched so the microwires protrude slightly from the NCG **32**. This is similar to the manner used to form the protruding electrodes on the curved side **64** of the NCG **32**.

A conceptual layout of the multiplexer **34** is shown in **Figure 4**. The silicon multiplexer **34** performs several operations in a sequential order. During the first step, an image is read onto the multiplexer **34**, pixel-by-pixel to each unit cell **72**. The row shift register **74** and column shift register **76** control the routing into each unit cell **72**. The discrete samples of analog video are input and stored as charge on MOS capacitor. This operation occurs every 60th of a second in a manner compatible with a RS-170 television format allowing the use of the test prosthesis **30** with standard video equipment. A multiplexer **34** that has a read-on and read-off capability has several input signals including a pixel clock, start-of-frame clock, bias voltage, ground, and analog input (RS-170). A digital electronics block **78** is of major importance because it generates switching pulses that routes image data into the unit cells **72** by controlling the row shift register **74** and the column shift register **76**. Without the on-chip digital electronics **78**, there might be a dozen or more clocks that would need to be input to the device. That would make the cable **27** from external drive electronics **25** through the eye wall **29** (as shown in **Figure 2**) much larger and more cumbersome. The use of IRFPA multiplexer technology greatly simplifies cable **27** problems through the eye wall **29**.

Referring again to **Figure 4**, after all the unit cells **72** have been loaded with the pixel values for the current frame, the next step is to send a biphasic pulse to that unit cell **72** which in

5 turn is modulated in proportion to the pixel value stored in each unit cell 72. Because the
biphasic pulse flows in parallel from a global external connection, the adjacent retinal neurons
are all stimulated simultaneously. This is an important feature of the design because it is
synchronistic action analogous to imaged photons stimulating photoreceptors in a normal retina.
Finally, the electrodes are all connected to ground to prevent any possible charge build up at the
10 electrode-neuron interface.

There are several important consideration in designing a device that performs all these
operations successfully. First the multiplexer 32 operation should be designed with many of the
requirements that exist for an IRFPA, for example, good uniformity, low noise, and high
dynamic range. Of course, the retinal prosthesis test device 30 moves image data in the opposite
15 direction than an IRFPA multiplexer, that is, image data moves onto the device rather than off
the device, but otherwise the specifications are analogous. **Figure 5** shows a generic design for a
unit cell 72. Note that the unit cell 72 stores the pixel value and then uses it to modulate the
biphasic pulse 82 that is input to the retinal tissue 54 through the NCG 32. Note that the
biphasic pulse 82 and the image data 84 are both generated off-chip. This allows for greater
20 flexibility during human testing as any image sequence can be input and combined with any
shape of biphasic pulse 82. The switch 86 at the bottom of **Figure 5** provides the capability to
connect the retinal tissue 54 to ground 88 to avoid any possibility of charge build-up.

Referring to **Figure 6**, the operation of the retinal prosthesis test device 30 during acute
experiments is controlled and powered by external ancillary electronics 25. The input signal is

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an image sequence at data rates fast enough to achieve 60 frames per second. The multiplexer **34** is designed to sample the multiplexed input signal in a manner compatible with the RS-170 format. This allows the retinal prosthesis test device **30** to be interfaced directly with any standard video camera. This includes the use of a computer which stores digital imagery and can display sequential fields at a 60 Hz rate (RS-170 interlaces two fields per frame at a rate of 30 frames per second). The actual control of the microelectronic multiplexer **34** is done with precisely timed pulses generated by a set of signal clocking boards **96** in a manner similar to that used in typical IRFPA's. The sync pulse generator **92** is used to synchronize the RS-170 signal **91** with the clocking pulses **96**. Basically, the sync pulse generator **92** detects the beginning of each RS-170 field and then sends a corresponding pulse to the drive electronics **94** that triggers the clocking signals **96** required to control each field of the image data input to the multiplexer **34**, synchronizaton of the pulses can be monitored with an oscilloscope **93**. The isolated breakout box **98** electrically isolates the human subject from high voltage power supplies. The box **98** contains opto-couplers that isolate the clock **96** and biphasic pulse signals **82** and low voltage batteries supplying bias potentials **102**.

The biphasic pulses **82** used to stimulate the retinal tissue **54** may be programmable such that any pulse shapes can be tested. This has several important implications for the development process. First, because the input impedance to the retinal tissue **54** has both a resistive and capacitive reactance associated with it, a square wave voltage pulse will not produce the desired square wave current pulse. Neurobiologists tend to favor square wave current pulses to achieve

5 efficient neural stimulation. With knowledge of the output impedance at the electrode-retina interface, a voltage shape can be computed that will provide a square wave current pulse, thus providing efficient stimulation. Second, there is evidence that various layers of the retina **54** can be stimulated with different shaped pulses - probably because of their differing frequency responses. Specifically, it is expected that either the ganglion or bipolar cells can be selectively
10 stimulated. Stimulating the bipolar cells instead of the ganglion cells has the advantage of reaching more deeply into the retina **54**, allowing a more natural form of stimulation.

Direct electrical stimulation of the ganglion cells precludes certain processing functions that normally would have occurred in the earlier layers of the retina **54**. Therefore, it may be necessary to perform certain functions on the incoming imagery before stimulation to
15 compensate for the missing processing. Unfortunately, a detailed model of human retinal functions has never been confirmed. Nevertheless, it has been shown that many intracellular recordings from the retinas of rabbits are very similar in mammalian vertebrate species in general.

In another preferred embodiment, a permanent implant device **40**, as shown in **Figure 7**, that is fully self-contained and responds to incident photons naturally imaged through the lens of
20 the eye, similar to that shown in **Figures 1c** and **1d**, is taught. The device **40** is surgically implanted in a patient's eye and has with no external connections passing through the eye wall. The basic design of this device **40** is based extensively on the retinal prosthesis test device **30** taught above. Specifically, the permanent implant device **40** would use a NCG array **102** hybridized to a silicon chip **104** in an identical manner to the retinal prosthesis test device **30**.

5 However, the unit cell **106** circuitry is redesigned because the image is no longer being multiplexed onto the chip through a cable from an external camera, but instead, the image is simultaneously generated within each unit cell **106** through a photon-to-electron conversion using a silicon photodiode **108**, as shown conceptually in **Figure 8**. The photons **112** propagate directly into each unit cell **106** because the silicon chip **104** is used in a back-illuminated
10 configuration -- essentially the photons **112** enter through the backside of the silicon chip **104**.

Packaging the device **40**, obviously, differs from that of the retinal prosthesis test device **30**. Packaging the permanent implant device **40** requires that the photons **112** be allowed to pass through the backside of the device **40**. This is a simple matter of eliminating the ceramic carrier taught in the retina prosthesis test device **30**. Thinning the silicon chip **104** is necessary because
15 of the need for good quantum efficiency. The packaging scheme for the permanent implant device **40** is shown in **Figure 7**. Note that the silicon chip **104** can be thinned to a few tens of microns so that the overall mass of the object is primarily that of the NCG array **102** making it more amenable for surgical attachment to the retina **114**.

It will be noted that there is no need for any multiplexing functions in the permanent
20 implant device **40**, therefore the design of the chip **104** is much simpler. Also there are no ancillary electronics, however, the silicon chip **104** significantly differs from that previously set forth, as shown in **Figure 9**. Although there are no multiplexing requirements, there are two new requirements, Specifically, these are external power and command signals necessary to adjust the operation of the device **40**. Transmitting power and signals onto the device **40** are

5 implemented with an inductively driven coil or antenna 116. The major on-chip electronic
adjustments needed are control of bias supplies 118 and biphasic pulse generator 122 plus the
standard digital electronics 124 that supply timing for the simultaneous operation of the unit cell
106 sequences. Again the operation of the device 40 is to collect charge in the storage capacitors
of the unit cells. The on-chip power receiver 126 provides conditioned power to operate all the
10 on-chip electronics. The frame rate would be nominally 60 frames per second, but because there
is no longer a need to be compatible with the RS-170 format, the frame rate could be adjusted to
anything desired.

Packaging of the permanent implant device 40 is very demanding. Along with issues of
biocompatibility is the question of device lifetime. Permanent implants might need to operate for
15 several decades. Similar requirements exist for other electronic implants such as cardiac
pacemakers and cochlear prosthetics. The encapsulation of the permanent implant device 40 is
easier in one respect than that of the retinal prosthesis test device 30 there are no connecting
cables to the device 40. In the case of the latter device 30, encapsulation was not a critical issue
because the duration of the experiments are typically less than one hour. Cables connected to any
20 neural prosthesis are subject to mechanical forces that over time can damage seals and ultimately
cause failures. Because the permanent implant device 40 is completely wireless (no cable
connections), simple encapsulation should be achievable with high integrity.

The specific teachings of this approach to neural implants is a new intra ocular device,
and has several extremely important advantages over any device taught by the prior art. First, the

5 use of the NCG enables the creation of a curved surface allowing the positioning of the
electrodes in extremely close proximity to the retinal cells over a large area. NCG also allows
the creation of very small electrodes (on the order of a micron) with very high densities
(thousands of electrodes per square millimeter). Regarding the multiplexer for the retinal
prosthesis test device **30**, as well as the unit cell size for the permanent implant device **40**, the
10 unit cell size can be made as small as practical based on the latest microelectronic design rules.

The multiplexer technology taught in the retinal prosthesis test device **30** uses only a
small number of electrical leads through the eye wall while allowing a high data rate to the retina.
In essence, this allows the input of image sequences to the retina, at high resolution and rapid
frame rates. The electrical leads may be fabricated on a small and flexible microcable. This is
15 critical to performing human experiments and testing. This is in comparison to directly coupling
all stimulating electrodes to individual leads. For example, a simple 8 x 8 test array when
directly coupled to input electronics outside the eye would require **64** input leads. The cabling
and accompanying connectors for such a device becomes very cumbersome.

The devices taught here **30** and **40** basically solves the technical problems of an earlier
20 concept envisioned by the research group at the Wilmer Ophthalmological Institute working with
North Carolina State University (NCSU). An approach similar to NCSU is also under study by
an MIT/Harvard team. Other efforts are proceeding in the United States, Germany and Japan that
build on the basic idea of stimulating retinal cells with a small number of electrodes on a
microelectronic chip. However, none of these approaches addresses the difficult issue of high-

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5 density electrodes in close proximity to the retina for achieving very high-resolution imagery.

A second approach is to stimulate the retina with a microelectronic chip from behind the retina, either replacing the diseased photoreceptors or positioning the chip just behind them.

A third approach is to skip the retina altogether and stimulate the visual center of the brain. In this approach, an array, with penetrating microelectrodes is positioned against a visual cortex.

10 This involves invasive brain surgery through the cranium. From a surgical point of view, the intra ocular approach is the least invasive.

Although this invention has been described in relation to an exemplary embodiment thereof, it will be understood by those skilled in the art that still other variations and modifications can be affected in the preferred embodiment without detracting from the scope and
15 spirit of the invention as described in the claims.